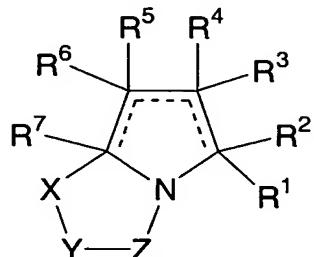


In the claims:

1. (Original) A compound of Formula I:



or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

- a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
n is 0 or 1;
r is 0 or 1;
s is 0 or 1;
u is 2, 3, 4 or 5;

a dashed line represents an optional double bond, provided that one and only one double bond is present in the ring;

X is selected from -CH₂- , -CH₂CH₂- , -SO₂- and -C(=O)-;

Y is selected from: O, N(R^c), S, -C(=O)-, -CH(R⁸)-, -N(R^c)C(=O)- and -N(R^c)CH(R⁸)-;
or

X and Y are combined to form -C(R⁸)=C(R⁸)-;

Z is selected from: -C(=O)-, -C(=S)-, -SO₂- and -C(R⁸)(R⁹)-,

R¹ and R⁵ are independently selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,

- 3) C₃-C₈ cycloalkyl, and
- 4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R², R³, R⁴, R⁶ and R⁷ are independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 7) C₁-C₆ aralkyl,
- 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰; or

R³ and R⁴ attached to the same carbon atom are combined to form -(CH₂)_u- wherein one of the carbon atoms is optionally replaced by a moiety selected from O, S(O)_m,

-N(R^a)C(O)-, -N(R^b)- and -N(COR^a)-;

R⁸and R⁹is independently selected from:

- 1) H,
- 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) (C=O)_aO_baryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) (C=O)_aO_b heterocyclyl,
- 7) CO₂H,
- 8) halo,
- 9) CN,
- 10) OH,
- 11) O_bC₁-C₆ perfluoroalkyl,

- 12) $O_a(C=O)_bNR^{12}R^{13}$,
- 13) $S(O)_mR^a$,
- 14) $S(O)_2NR^{12}R^{13}$,
- 15) CHO,
- 16) $(N=O)R^{12}R^{13}$, and
- 17) $(C=O)_aO_bC_3-C_8$ cycloalkyl,

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R¹⁰ is independently selected from:

- 1) $(C=O)_aO_bC_1-C_{10}$ alkyl,
- 2) $(C=O)_aO_b$ aryl,
- 3) C_2-C_{10} alkenyl,
- 4) C_2-C_{10} alkynyl,
- 5) $(C=O)_aO_b$ heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR¹²R¹³,
- 12) S(O)_mR^a,
- 13) S(O)₂NR¹²R¹³,
- 14) oxo,
- 15) CHO,
- 16) $(N=O)R^{12}R^{13}$,
- 17) $(C=O)_aO_bC_3-C_8$ cycloalkyl, and
- 18) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R¹¹ is selected from:

- 1) $(C=O)_rO_s(C_1-C_{10})$ alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,

- 3) (C_0-C_6) alkylene-S(O)_mR^a,
- 4) oxo,
- 5) OH,
- 6) halo,
- 7) CN,
- 8) (C=O)_rO_s(C₂-C₁₀)alkenyl,
- 9) (C=O)_rO_s(C₂-C₁₀)alkynyl,
- 10) (C=O)_rO_s(C₃-C₆)cycloalkyl,
- 11) (C=O)_rO_s(C₀-C₆)alkylene-aryl,
- 12) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl,
- 13) (C=O)_rO_s(C₀-C₆)alkylene-N(R^b)₂,
- 14) C(O)R^a,
- 15) (C₀-C₆)alkylene-CO₂R^a,
- 16) C(O)H,
- 17) (C₀-C₆)alkylene-CO₂H,
- 18) C(O)N(R^b)₂,
- 19) S(O)_mR^a,
- 20) S(O)₂N(R^b)₂ and
- 21) -OPO(OH)₂;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

R¹² and R¹³ are independently selected from:

- 1) H,
- 2) (C=O)O_bC₁-C₁₀ alkyl,
- 3) (C=O)O_bC₃-C₈ cycloalkyl,
- 4) (C=O)O_baryl,
- 5) (C=O)O_bheterocyclyl,
- 6) C₁-C₁₀ alkyl,
- 7) aryl,
- 8) C₂-C₁₀ alkenyl,
- 9) C₂-C₁₀ alkynyl,
- 10) heterocyclyl,

- 11) C₃-C₈ cycloalkyl,
- 12) SO₂R^a, and
- 13) (C=O)NR^b₂,

said alkyl, cycloalkyl, aryl, heterocyl, alkenyl, and alkynyl is optionally substituted with one or more substituents selected from R¹¹, or

R¹² and R¹³ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one or more substituents selected from R¹¹;

R¹⁴ is independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR¹²R¹³,
- 12) S(O)_mR^a,
- 13) S(O)₂NR¹²R¹³,
- 14) oxo,
- 15) CHO,
- 16) (N=O)R¹²R¹³,
- 17) (C=O)_aO_bC₃-C₈ cycloalkyl, and
- 18) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl, optionally substituted with one to three substituents selected from R¹⁴;

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl or S(O)₂R^a, optionally substituted with one to three substituents selected from R¹⁴;

R^c and R^{c'} are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl, optionally substituted with one, two or three substituents selected from R¹⁰, or

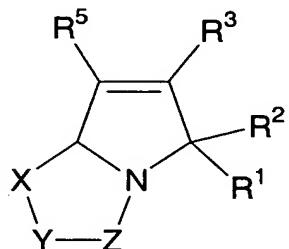
R^c and R^{c'} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 3-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^d and R^{d'} are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^b₂, or

R^d and R^{d'} can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NR^e, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹; and

R^e is selected from: H and (C₁-C₆)alkyl.

2. (Original) The compound according to Claim 1 of the Formula II:



II

or a pharmaceutically acceptable salt or stereoisomer thereof,

wherein:

a is 0 or 1;
b is 0 or 1;
m is 0, 1, or 2;
n is 0 or 1;
r is 0 or 1;
s is 0 or 1;

X is selected from -CH₂- and -CH₂CH₂-;

Y is selected from: O, N(R^c), S, -C(=O)-, -CH(R⁸)-, -N(R^c)C(=O)- and -N(R^c)CH(R⁸)-;

Z is selected from: -C(=O)-, -C(=S)-, -SO₂- and -C(R⁸)(R⁹)-,

R¹ and R⁵ are independently selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,
- 3) C₃-C₈ cycloalkyl, and
- 4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R² and R³ are independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 7) C₁-C₆ aralkyl,
- 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R⁸and R⁹is independently selected from:

- 1) H,
- 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) (C=O)_aO_baryl,
- 4) (C=O)_aO_b heterocyclyl,
- 5) CO₂H,
- 6) halo,
- 7) CN,
- 8) OH,
- 9) O_bC₁-C₆ perfluoroalkyl,
- 10) O_a(C=O)_bNR¹²R¹³, and
- 11) (C=O)_aO_bC₃-C₈ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R¹⁰ is independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR¹²R¹³,
- 12) S(O)_mR^a,
- 13) S(O)₂NR¹²R¹³,
- 14) oxo,
- 15) CHO,
- 16) (N=O)R¹²R¹³,

- 17) $(C=O)_a O_b C_3-C_8$ cycloalkyl, and
- 18) $-OPO(OH)_2;$

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R¹¹;

R¹¹ is selected from:

- 1) $(C=O)_r O_s (C_1-C_{10})$ alkyl,
- 2) $O_r (C_1-C_3)$ perfluoroalkyl,
- 3) oxo,
- 4) OH,
- 5) halo,
- 6) CN,
- 7) (C_2-C_{10}) alkenyl,
- 8) (C_2-C_{10}) alkynyl,
- 9) $(C=O)_r O_s (C_3-C_6)$ cycloalkyl,
- 10) $(C=O)_r O_s (C_0-C_6)$ alkylene-aryl,
- 11) $(C=O)_r O_s (C_0-C_6)$ alkylene-heterocyclyl,
- 12) $(C=O)_r O_s (C_0-C_6)$ alkylene-N(R^b)₂,
- 13) C(O)R^a,
- 14) (C_0-C_6) alkylene-CO₂R^a,
- 15) C(O)H,
- 16) (C_0-C_6) alkylene-CO₂H,
- 17) C(O)N(R^b)₂,
- 18) S(O)_mR^a,
- 19) S(O)₂N(R^b)₂, and
- 20) $-OPO(OH)_2;$

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, alkylene and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

R¹² and R¹³ are independently selected from:

- 1) H,
- 2) $(C=O)O_b C_1-C_{10}$ alkyl,
- 3) $(C=O)O_b C_3-C_8$ cycloalkyl,

- 4) (C=O)Obaryl,
- 5) (C=O)Obheterocyclyl,
- 6) C₁-C₁₀ alkyl,
- 7) aryl,
- 8) C₂-C₁₀ alkenyl,
- 9) C₂-C₁₀ alkynyl,
- 10) heterocyclyl,
- 11) C₃-C₈ cycloalkyl,
- 12) SO₂R^a, and
- 13) (C=O)NR^b₂,

said alkyl, cycloalkyl, aryl, heterocylyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R¹¹, or

R¹² and R¹³ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl;

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl,(C=O)C₁-C₆ alkyl or S(O)₂R^a;

R^c and R^{c'} are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl; or

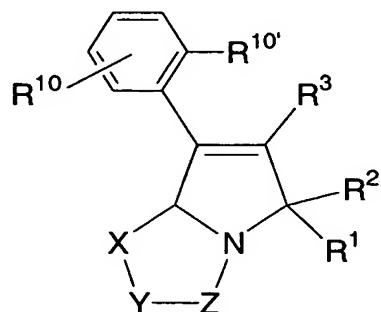
R^c and R^{c'} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^d and R^{d'} are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^b₂, or

R^d and $R^{d'}$ can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NRE, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R^{11} ; and

R^e is selected from: H and (C₁-C₆)alkyl.

3. (Original) The compound according to Claim 2 of Formula III:



III

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

- a is 0 or 1;
- b is 0 or 1;
- m is 0, 1, or 2;
- r is 0 or 1;
- s is 0 or 1;

X is selected from -CH₂- and -CH₂CH₂-;

Y is selected from: O, N(R^c), S, -CH(R⁸)- and -N(R^c)CH(R⁸)-;

Z is selected from: -C(=O)-, -C(=S)-, -SO₂- and -C(R⁸)(R⁹)-,

R^1 is selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,

- 3) C₃-C₈ cycloalkyl, and
- 4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R² and R³ are independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 7) C₁-C₆ aralkyl,
- 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R⁸and R⁹is independently selected from:

- 1) H,
- 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) CO₂H,
- 4) halo,
- 5) OH,
- 6) O_a(C=O)_bNR¹²R¹³, and
- 7) (C=O)_aO_bC₃-C₈ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R¹⁰ is independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,

- 5) $(C=O)_a O_b$ heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR₁₂R₁₃,
- 12) S(O)_mR^a,
- 13) S(O)₂NR₁₂R₁₃,
- 14) oxo,
- 15) CHO,
- 16) (N=O)R₁₂R₁₃,
- 17) (C=O)_aO_bC₃-C₈ cycloalkyl, and
- 18) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R¹¹;

R^{10'} is halogen;

R¹¹ is selected from:

- 1) (C=O)_rO_s(C₁-C₁₀)alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 3) oxo,
- 4) OH,
- 5) halo,
- 6) CN,
- 7) (C₂-C₁₀)alkenyl,
- 8) (C₂-C₁₀)alkynyl,
- 9) (C=O)_rO_s(C₃-C₆)cycloalkyl,
- 10) (C=O)_rO_s(C₀-C₆)alkylene-aryl,
- 11) (C=O)_rO_s(C₀-C₆)alkylene-heterocyclyl,
- 12) (C=O)_rO_s(C₀-C₆)alkylene-N(R^b)₂,
- 13) C(O)R^a,
- 14) (C₀-C₆)alkylene-CO₂R^a,

- 15) C(O)H,
- 16) (C₀-C₆)alkylene-CO₂H,
- 17) C(O)N(R^b)₂,
- 18) S(O)_mR^a,
- 19) S(O)₂N(R^b)₂, and
- 20) -OP(OH)₂;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from R^b, OH, (C₁-C₆)alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

R¹² and R¹³ are independently selected from:

- 1) H,
- 2) (C=O)O_bC₁-C₁₀ alkyl,
- 3) (C=O)O_bC₃-C₈ cycloalkyl,
- 4) (C=O)O_baryl,
- 5) (C=O)O_bheterocyclyl,
- 6) C₁-C₁₀ alkyl,
- 7) aryl,
- 8) C₂-C₁₀ alkenyl,
- 9) C₂-C₁₀ alkynyl,
- 10) heterocyclyl,
- 11) C₃-C₈ cycloalkyl,
- 12) SO₂R^a, and
- 13) (C=O)NR^b₂,

said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R¹¹, or R¹² and R¹³ can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl;

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl,(C=O)C₁-C₆ alkyl or S(O)₂R^a;

R^c and R^{c'} are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocycll and (C₃-C₆)cycloalkyl; or

R^c and R^{c'} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^d and R^{d'} are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^b₂, or

R^d and R^{d'} can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NR^e, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹; and R^e is selected from: H and (C₁-C₆)alkyl.

4. (Original) The compound according to Claim 3 of the Formula III, or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

X is selected from -CH₂- and -CH₂CH₂-;

Y is selected from: O, N(R^c), -CH(R⁸)- and -N(R^c)CH(R⁸)-;

Z is selected from: -C(=O)- and -SO₂-;

R¹ is selected from:

- 1) aryl, and
- 2) heteroaryl,

said aryl and heteroaryl is optionally substituted with one or more substituents selected from R¹⁰;

R² and R³ are independently selected from:

- 1) H, and
- 2) C₁-C₁₀ alkyl,

said alkyl is optionally substituted with one or more substituents selected from R¹⁰; and

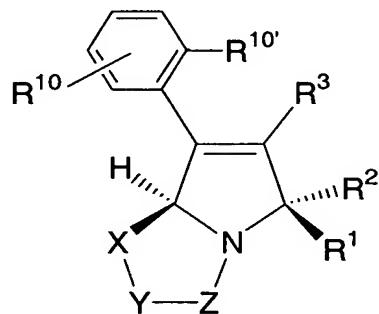
R⁸and R⁹is independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) OH,
- 4) NR¹²R¹³, and
- 5) C₃-C₈ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

X, Y, Z, R¹⁰, R^{10'}, R¹¹, R¹², R¹³, R^a, R^b, R^c and R^{c'} are as described in Claim 3.

5. (Original) The compound according to Claim 4 of the Formula IV,



IV

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein

- a is 0 or 1;
- b is 0 or 1;
- m is 0, 1, or 2;
- r is 0 or 1;
- s is 0 or 1;

X is selected from -CH₂- and -CH₂CH₂-;

Y is selected from: O, N(R^c), S, -CH(R⁸)- and -N(R^c)CH(R⁸)-;

Z is selected from: -C(=O)- and -SO₂-;

R¹ is selected from:

- 1) aryl,
- 2) C₁-C₆ aralkyl,
- 3) C₃-C₈ cycloalkyl, and
- 4) heterocyclyl,

said aryl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R² is independently selected from:

- 1) H,
- 2) C₁-C₁₀ alkyl,
- 3) aryl,
- 4) C₂-C₁₀ alkenyl,
- 5) C₂-C₁₀ alkynyl,
- 6) C₁-C₆ perfluoroalkyl,
- 7) C₁-C₆ aralkyl,
- 8) C₃-C₈ cycloalkyl, and
- 9) heterocyclyl,

said alkyl, aryl, alkenyl, alkynyl, cycloalkyl, aralkyl and heterocyclyl is optionally substituted with one or more substituents selected from R¹⁰;

R³ is H;

R⁸ is independently selected from:

- 1) H,
- 2) (C=O)_aO_bC₁-C₁₀ alkyl,
- 3) CO₂H,
- 4) halo,
- 5) OH,
- 6) O_a(C=O)_bNR¹²R¹³, and
- 7) (C=O)_aO_bC₃-C₈ cycloalkyl,

said alkyl, aryl, heterocyclyl, and cycloalkyl optionally substituted with one or more substituents selected from R¹¹;

R¹⁰ is independently selected from:

- 1) (C=O)_aO_bC₁-C₁₀ alkyl,
- 2) (C=O)_aO_baryl,
- 3) C₂-C₁₀ alkenyl,
- 4) C₂-C₁₀ alkynyl,
- 5) (C=O)_aO_b heterocyclyl,
- 6) CO₂H,
- 7) halo,
- 8) CN,
- 9) OH,
- 10) O_bC₁-C₆ perfluoroalkyl,
- 11) O_a(C=O)_bNR¹²R¹³,
- 12) S(O)_mR^a,
- 13) S(O)₂NR¹²R¹³,
- 14) oxo,
- 15) CHO,
- 16) (N=O)R¹²R¹³,
- 17) (C=O)_aO_bC₃-C₈ cycloalkyl, and
- 18) -OPO(OH)₂;

said alkyl, aryl, alkenyl, alkynyl, heterocyclyl, and cycloalkyl optionally substituted with one, two or three substituents selected from R¹¹;

R^{10'} is halogen;

R¹¹ is selected from:

- 1) (C=O)_rO_s(C₁-C₁₀)alkyl,
- 2) O_r(C₁-C₃)perfluoroalkyl,
- 3) oxo,
- 4) OH,
- 5) halo,
- 6) CN,
- 7) (C₂-C₁₀)alkenyl,
- 8) (C₂-C₁₀)alkynyl,
- 9) (C=O)_rO_s(C₃-C₆)cycloalkyl,

- 10) $(C=O)_r O_s (C_0-C_6)$ alkylene-aryl,
- 11) $(C=O)_r O_s (C_0-C_6)$ alkylene-heterocyclyl,
- 12) $(C=O)_r O_s (C_0-C_6)$ alkylene-N(R^b)₂,
- 13) C(O) R^a ,
- 14) (C_0-C_6) alkylene-CO₂ R^a ,
- 15) C(O)H,
- 16) (C_0-C_6) alkylene-CO₂H,
- 17) C(O)N(R^b)₂,
- 18) S(O)_m R^a ,
- 19) S(O)₂N(R^b)₂, and
- 20) -OPO(OH)₂;

said alkyl, alkenyl, alkynyl, cycloalkyl, aryl, and heterocyclyl is optionally substituted with up to three substituents selected from R^b , OH, (C_1-C_6) alkoxy, halogen, CO₂H, CN, O(C=O)C₁-C₆ alkyl, oxo, and N(R^b)₂;

R^{12} and R^{13} are independently selected from:

- 1) H,
- 2) $(C=O)O_b C_1-C_{10}$ alkyl,
- 3) $(C=O)O_b C_3-C_8$ cycloalkyl,
- 4) $(C=O)O_b$ aryl,
- 5) $(C=O)O_b$ heterocyclyl,
- 6) C_1-C_{10} alkyl,
- 7) aryl,
- 8) C_2-C_{10} alkenyl,
- 9) C_2-C_{10} alkynyl,
- 10) heterocyclyl,
- 11) C_3-C_8 cycloalkyl,
- 12) SO₂ R^a , and
- 13) $(C=O)NR^b_2$,

said alkyl, cycloalkyl, aryl, heterocyclyl, alkenyl, and alkynyl is optionally substituted with one, two or three substituents selected from R^{11} , or

R^{12} and R^{13} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the

nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^a is (C₁-C₆)alkyl, (C₃-C₆)cycloalkyl, aryl, or heterocyclyl;

R^b is H, (C₁-C₆)alkyl, aryl, heterocyclyl, (C₃-C₆)cycloalkyl, (C=O)OC₁-C₆ alkyl, (C=O)C₁-C₆ alkyl or S(O)₂R^a;

R^c and R^{c'} are independently selected from: H, (C₁-C₆)alkyl, aryl, heterocyclyl and (C₃-C₆)cycloalkyl; or

R^c and R^{c'} can be taken together with the nitrogen to which they are attached to form a monocyclic or bicyclic heterocycle with 5-7 members in each ring and optionally containing, in addition to the nitrogen, one or two additional heteroatoms selected from N, O and S, said monocyclic or bicyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹;

R^d and R^{d'} are independently selected from: (C₁-C₆)alkyl, (C₁-C₆)alkoxy and NR^b₂, or

R^d and R^{d'} can be taken together with the phosphorous to which they are attached to form a monocyclic heterocycle with 5-7 members the ring and optionally containing, in addition to the phosphorous, one or two additional heteroatoms selected from NR^e, O and S, said monocyclic heterocycle optionally substituted with one, two or three substituents selected from R¹¹; and

R^e is selected from: H and (C₁-C₆)alkyl.

6. (Original) A compound selected from:

(±)-(5S,7aR and 5R,7aS)-7-(2,5-Difluorophenyl)-5-phenyl-2,7a-dihydro-1H-pyrrole[1,2-c][1,3]oxazol-3-one;

(±)-(5S,7aS and 5R,7aR)-7-(2,5-Difluorophenyl)-5-phenyl-2,7a-dihydro-1H-pyrrole[1,2-c][1,3]oxazol-3-one;

(±)-7-(2,5-Difluorophenyl)-5-phenyl-1,2,5,7a-tetrahydro-3H-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(5*S*,7*aR*)-7-(2,5-Difluorophenyl)-2-methyl-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(5*S*,7*aR*)-7-(2,5-Difluorophenyl)-2-ethyl-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(5*S*,7*aR*)-7-(2,5-Difluorophenyl)-2-[2-(dimethylamino)ethyl]-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(5*S*,7*aR*)-7-(2,5-Difluorophenyl)-2-[2-(diethylamino)ethyl]-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(5*S*,7*aR*)-7-(2,5-Difluorophenyl)-2-cyclopropyl-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-c]imidazol-3-one;

(\pm)-(2*S,5R* and 2*R,5S*)-7-(2,5-Difluorophenyl)-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-a]pyrazin-4(1*H*)-one;

(\pm)-(2*S,5S* and 2*R,5R*)-7-(2,5-Difluorophenyl)-5-phenyl-1,2,5,7*a*-tetrahydro-3*H*-pyrrolo[1,2-a]pyrazin-4(1*H*)-one

(\pm)-(6*S,8aR* and 6*R,8aS*)-8-(2,5-Difluorophenyl)-2-methyl-6-phenyl-2,3,6,8*a*-tetrahydropyrrolo[1,2-a]pyrazin-4(1*H*)-one; and

(\pm)-(6*S,8aR* and 6*R,8aS*)-8-(2,5-Difluorophenyl)-6-phenyl-1,2,6,8*a*-tetrahydropyrrolo [1,2-a]pyrazin-3(4*H*)-one;

or a pharmaceutically acceptable salt or stereoisomer thereof.

7. (Original) A pharmaceutical composition that is comprised of a compound in accordance with Claim 1 and a pharmaceutically acceptable carrier.

8. (Original) A method of treating or preventing cancer in a mammal in need of such treatment that is comprised of administering to said mammal a therapeutically effective amount of a compound of Claim 1.

9. (Original) A method of treating cancer or preventing cancer in accordance with Claim 8 wherein the cancer is selected from cancers of the brain, genitourinary tract, lymphatic system, stomach, larynx and lung.

10. (Original) A method of treating or preventing cancer in accordance with Claim 8 wherein the cancer is selected from histiocytic lymphoma, lung adenocarcinoma, small cell lung cancers, pancreatic cancer, glioblastomas and breast carcinoma.

11. (Cancelled)

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

16. (Cancelled)

17. (Cancelled)

18. (Cancelled)

19. (Cancelled)

20. (Cancelled)

21. (Original) A method of treating or preventing cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with a compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) a retinoid receptor modulator,

- 4) a cytotoxic/cytostatic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor,
- 10) an angiogenesis inhibitor,
- 11) PPAR- γ agonists,
- 12) PPAR- δ agonists,
- 13) an inhibitor of inherent multidrug resistance,
- 14) an anti-emetic agent,
- 15) an agent useful in the treatment of anemia,
- 16) an agent useful in the treatment of neutropenia,
- 17) an immunologic-enhancing drug,
- 18) an inhibitor of cell proliferation and survival signaling, and
- 19) an agent that interferes with a cell cycle checkpoint.

22. (Original) A method of treating cancer that comprises administering a therapeutically effective amount of a compound of Claim 1 in combination with radiation therapy and a compound selected from:

- 1) an estrogen receptor modulator,
- 2) an androgen receptor modulator,
- 3) a retinoid receptor modulator,
- 4) a cytotoxic/cytostatic agent,
- 5) an antiproliferative agent,
- 6) a prenyl-protein transferase inhibitor,
- 7) an HMG-CoA reductase inhibitor,
- 8) an HIV protease inhibitor,
- 9) a reverse transcriptase inhibitor,
- 10) an angiogenesis inhibitor,
- 11) PPAR- γ agonists,
- 12) PPAR- δ agonists,
- 13) an inhibitor of inherent multidrug resistance,
- 14) an anti-emetic agent,
- 15) an agent useful in the treatment of anemia,

- 16) an agent useful in the treatment of neutropenia,
- 17) an immunologic-enhancing drug,
- 18) an inhibitor of cell proliferation and survival signaling, and
- 19) an agent that interferes with a cell cycle checkpoint.

23. (Cancelled)

24. (Cancelled)

25. (Cancelled)

26. (Cancelled)

27. (Cancelled)

28. (Cancelled)

29. (Cancelled)

30. (Cancelled)

31. (Cancelled)

32. (Original) A method of modulating mitotic spindle formation which comprises administering a therapeutically effective amount of a compound of Claim 1.

33. (Original) A method of inhibiting the mitotic kinesin KSP which comprises administering a therapeutically effective amount of a compound of Claim 1.